Assessing the role of Eph/ephrin signaling in hESC growth and differentiation

Grant Award Details

Assessing the role of Eph/ephrin signaling in hESC growth and differentiation

Grant Type: SEED Grant

Grant Number: RS1-00199

Investigator:

Name:	David Feldheim
Institution:	University of California, Santa Cruz
Type:	PI

Human Stem Cell Use: Embryonic Stem Cell

Award Value: $474,161

Status: Closed

Progress Reports

Reporting Period: Year 2

View Report

Reporting Period: NCE

View Report

Grant Application Details

Application Title: Assessing the role of Eph/ephrin signaling in hESC growth and differentiation

Public Abstract:

An important aspect of understanding stem cell biology is to have a basic understanding of the processes that balance stem cell self-renewal and differentiation. Stem cell proliferation and differentiation signals are at least partially regulated by direct contact between cells. For example, stem cells normally reside in a specific microenvironment, or "niche", that integrates specific cell-cell contacts in order to translate information from the environment into proliferation patterns. In this SEED proposal we plan to investigate the role of Eph/ephrin signaling in hESC growth and differentiation. Eph receptor tyrosine kinases and their ligands, ephrins, are large gene families that initiate signal transduction pathways which lead to changes in cellular adhesion, proliferation, and migration. Both Ephs and ephrins are expressed on the surfaces of cells, thus restricting their interactions to sites of direct cell-cell contact. It is known that Ephs and ephrins are expressed in hESCs and are therefore in the right place to be involved in regulating hESC proliferation and differentiation decisions. To better understand how Ephs and ephrins might be involved in hESC growth regulation, we plan to characterize the expression of Ephs and ephrins in hESCs during different stages of growth and neural differentiation to determine if Eph/ephrin signaling is used to regulate proliferation and differentiation of hESCs. The characterization of the role that Ephs and ephrins play in hESCs will provide insights into how stem cell proliferation is regulated in culture and will likely be applicable to how stem cell niches are organized in vivo. This understanding may allow for the development of standard culture conditions that will optimize both self-renewal and homogeneity of cells. This will in turn lead to more efficient large-scale production of stem cell populations and also methods for maintaining a self-renewing state in culture. Conversely, in a therapeutic setting, even a small number of undifferentiated cells could result in tumor formation; therefore, we also need to understand how to prevent self-renewal of stem cells.

Statement of Benefit to California:

This proposed research will benefit the State of California and it citizens by addressing the molecular signals that are involved in triggering human embryonic stems cells to divide, die, or differentiate into neurons. Human embryonic stem cells have great potential to be used in cell replacement therapies once their growth and differentiation programs are understood. Our work studying the role of a major class of signaling molecules, Ephs and ephrins, is likely to shed light on how these signals are generated and responded to in culture. Understanding how this process is regulated at the molecular level may allow for the development of standard culture conditions that will optimize both self-renewal and homogeneity of cells; which in turn can lead to the large-scale production of stem cell populations and methods for maintaining a self-renewing state by reversible blocking of hESCs. It is also important to make sure that upon differentiation, no stem cells are left behind, because they may be able to give rise to tumors when put into the body.
